

REMARKS/ARGUMENTS

Claims 26-32, 34, 36-38 and 48 are active in this application. Support for the amendment to Claim 26 is found in Claims 1-25 and the specification as originally filed. Support for Claim 48 is found in the sequence listing as well as the specification as originally filed. No new matter is added by these amendments.

Applicants affirm the election of Group III, Claims 26-38. The pending claims are drawn to the elected subject matter.

The rejection of Claims 26-38 under 35 U.S.C. § 112, first paragraph (written description) is respectfully traversed.

Claim 26, as amended herein, is directed to a process for producing L-amino acids with a bacterial cell containing an attenuated lysR3 gene which is defined as particular nucleic acid sequences prior to attenuation. As described on page 9, lines 8-11, "A bacterial strain with attenuated expression of a lysR3 gene encodes a polypeptide with LysR3 transcriptional regulation activity will improve amino acid yield at least 1%."

In addition, on page 7, line 29 through page 8, line 4, attenuation is defined as being "the reduction or elimination of the intracellular activity of one or more enzymes (proteins) in a microorganism which are coated by the corresponding DNA, for example, by using a weak promoter and using a gene or allele which codes for a corresponding enzyme with a low activity or inactivates the corresponding gene or enzyme (protein), and optionally combining these measures."

Achieving attenuation is described in the specification, starting on page 12, line 7, which states "To achieve an attenuation, either the expression of the lysR3 gene with catalytic properties of the enzyme protein can be reduced or eliminated. The two measures can optionally be combined."

Support for the hybridization conditions is found in Claim 8 and the specification on pages 11 and 12.

Withdrawal of this ground of rejection is requested.

The rejection of Claims 26-38 under 35 U.S.C. § 112, first paragraph (enablement) is similarly traversed.

The claims, as amended herein, define the lysR3 gene prior to attenuation as comprising SEQ ID NO:1, 3 or a polynucleotide which hybridizes to the full complement of these sequences provided it is capable of encoding a protein with LysR3 transcriptional regulatory activity.

The relevant disclosure for making such a bacterial cell, attenuating the gene, and the hybridization conditions are specifically identified above. Thus, one can unquestionably practice the claimed invention without undue experimentation.

Withdrawal of this ground of rejection is requested.

The rejection of Claims 29, 33 and 35 under 35 U.S.C. § 112, first paragraph, is respectfully traversed.

Claims 33 and 35 have been cancelled.

With respect to Claim 29, please note that these strains were known and described previously and are, in fact, publicly available. This public availability is illustrated by the fact that each strain has been designated with a deposit number. As further support, Applicants submit catalogue entries from the American Type Culture Collection (ATCC) for strains listed in Claim 29.

In view of the above, withdrawal of this ground of rejection is requested.

The rejection of Claims 26-38 under 35 U.S.C. § 112, second paragraph, is respectfully traversed.

Claim 26 has been amended to include the step "recovering the produced L-amino acid."

The essential inquiry pertaining to the requirement under 35 U.S.C. § 112, second paragraph is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

- (A) The content of the particular application disclosure;
- (B) The teachings of the prior art; and
- (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. See MPEP § 2173.02

The phrase "attenuated lysR3 gene" is defined in the claim and the specification (see page 9, lines 8-11; page 7, line 29 to page 8, line 4; and page 12, line 7).

The genes that are attenuated in Claim 38 are adequately definite in light of the definition of attenuated in the application coupled with the fact that the pck, pgi and poxB genes were (see the relevant references positioned next to each gene on page 16, lines 5-11).

Similarly, the genes listed in Claims 36 and 38 were also known as described on pages 15-16 of the application. As a result, enhancing the gene activity is the opposite of attenuating such that there is an increased level of gene activity relative to the normal levels or endogenous levels present in a bacterial cell.

Applicants request withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

Applicants request consideration of the Information Disclosure Statements filed on October 16, 2001 and November 20, 2001. Copies of these Information Disclosure Statement filings are enclosed for convenience. Therefore, a returned signed copy of the PTO Form 1449 from each of these IDS's is requested.

Application No. 09/867,537
Reply to Office Action of July 29, 2003

Applicants also request this application now be passed to issuance.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



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Bacteria	
ATCC Number:	13032 <input type="button" value="Order this item"/>
Price:	\$150.00
Organism:	<i>Corynebacterium glutamicum</i> (Kinoshita et al.) Abe et al. deposited as <i>Micrococcus glutamicus</i> Kinoshita et al.
Designations:	534 [NCIB 10025] Isolation: sewage
Depositors:	Kyowa Ferm. Ind. Co., Ltd.
Biosafety Level:	1 Shipped: freeze-dried
Growth Conditions:	ATCC medium: 3 Nutrient agar (Difco 0001) or nutrient broth (Difco 0003) Temperature: 37.0 C
<p>Permits/Forms: In addition to the MTA mentioned above, other ATCC and/or regulatory permits may be required for the transfer of this ATCC material. Anyone purchasing ATCC material is ultimately responsible for obtaining the permits. Please click here for information regarding the specific requirements for shipment to your location.</p> <p>This material is cited in a U.S. and/or other Patent or Patent Application, and may not be used to infringe on the patent claims.</p> <p style="text-align: right;"><u>Related Products</u></p>	
Type Strain:	type strain (type strain)
Comments:	genome sequencing strain lysine uptake and exchange [10717]
Applications:	produces glutamic acid [glutamate] [25644] [25654] [34142] [49877] transformation host
References:	<p>10717: Broer S, Kramer R. Lysine uptake and exchange in <i>Corynebacterium glutamicum</i>. J. Bacteriol. 172: 7241-7248, 1990. PubMed: 2123868</p> <p>25644: Sadao A, et al. Method of producing L-glutamic acid. US Patent 3,002,889 dated Oct 3 1961</p> <p>25654: Sadao A, et al. Microbiological production of amino acid by reductive amination. US Patent 3,220,929 dated Nov 30 1965</p> <p>32192: Tsuchida T, et al. Process for producing L-amino acids by fermentation. US Patent 5,705,370 dated Jan 6 1998</p> <p>34142: Kinoshita S, et al. Method of producing L-glutamic acid by fermentation. US</p>

	Patent 3,003,925 dated Oct 10 1961 36887: Skerman VB, et al. Approved lists of bacterial names. Int. J. Syst. Bacteriol. 30: 225-420, 1980. 49877: Kinoshita S, et al. Taxonomical study of glutamic acid accumulating bacteria, Micrococcus glutamicus nov. sp.. Bull. Agric. Chem. Soc. Jpn. 22: 176-185, 1958.
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13032	Word Search
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Bacteria	
ATCC Number:	15806 Order this item Price: \$190.00
Organism:	<i>Corynebacterium acetoglutamicum</i> Tanaka et al.
Designations:	KY 3513 Isolation: soil
Depositors:	Kyowa Ferm. Ind. Co., Ltd. History: ATCC<<--Kyowa Ferm. Ind. Co., Ltd. <<--K. Tanaka and K. Oshima
<u>Biosafety Level:</u>	1 Shipped: freeze-dried
Growth Conditions:	<u>ATCC medium:</u> 44 Brain heart infusion agar (Difco 0418) or brain heart infusion (Difco 0037) Temperature: 30.0 C
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<u>Related Products</u>	
Applications:	produces FAD [flavin-adenine dinucleotide] [2591] produces glutamic acid [glutamate] [2643]
References:	2591 : Tanaka M, et al.. Process for producing flavin-adenine dinucleotide. US Patent 3,647,627 dated Mar 7 1972 2643 : Tanaka K, et al.. Fermentative method for the production of L-glutamic acid. US Patent 3,335,065 dated Aug 8 1967

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Bacteria

ATCC Number:

13870

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Price:

\$190.00

Organism:

Corynebacterium acetoacidophilum Shii et al.

Designations:

410 [CIP 103776]

Depositors:

Ajinomoto Co., Inc.

**Biosafety
Level:**

1

Shipped:

freeze-dried

**Growth
Conditions:**

ATCC medium: 44 Brain heart infusion agar (Difco 0418) or brain heart infusion (Difco 0037)
Temperature: 37.0 C

Permits/Forms:

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Related Products

Comments:	taxonomic characterization [2635]
Applications:	produces glutamic acid [glutamate] [2635]
References:	2635: Shiio I, et al. Process for producing L-glutamic acid. US Patent 3,117,915 dated Jan 14 1964 32192: Tsuchida T, et al. Process for producing L-amino acids by fermentation. US Patent 5,705,370 dated Jan 6 1998

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Bacteria	
ATCC Number:	17965 Order this item Price: \$190.00
Organism:	<i>Corynebacterium melassecola</i> Goto et al.
Designations:	AS B-4821 Isolation: soil
Depositors:	Asahi Kasei Kogyo Kabushiki Kaisha
Biosafety Level:	1 Shipped: freeze-dried
Growth Conditions:	ATCC medium: 3 Nutrient agar (Difco 0001) or nutrient broth (Difco 0003) Temperature: 30.0 C
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Applications:	produces glutamic acid [glutamate] [2650] [2651]
References:	<p>2650: Goto T, et al. Process for producing L-glutamic acid by using <i>Corynebacterium melassecola</i>. US Patent 3,355,359 dated Nov 28 1967</p> <p>2651: Ohsawa T, et al.. Process for producing L-glutamic acid by using bacteria. US Patent 3,399,114 dated Aug 27 1968</p>

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Bacteria

ATCC Number:

14067

Price:

\$190.00

Organism:

Corynebacterium glutamicum (Kinoshita et al.) Abe et al. deposited as
Brevibacterium flavum Okumura et al.

Designations:

2247

Depositors:	Ajinomoto Co., Inc.		
Biosafety Level:	1	Shipped:	freeze-dried
Growth Conditions:	ATCC medium: 3 Nutrient agar (Difco 0001) or nutrient broth (Difco 0003) Temperature: 30.0 C		
Permits/Forms: In addition to the <u>MTA</u> mentioned above, other ATCC and/or regulatory permits may be required for the transfer of this ATCC material. Anyone purchasing ATCC material is ultimately responsible for obtaining the permits. Please click here for information regarding the specific requirements for shipment to your location. This material is cited in a U.S. and/or other Patent or Patent Application, and may not be used to infringe on the patent claims.			
<u>Related Products</u>			
Comments:	taxonomic characterization [49855]		
Applications:	produces glutamate synthase [57836] produces glutamic acid [glutamate] [2636] transformation host [8752]		
References:	2636: Motozaki S, et al. Process for producing L-glutamic acid. US Patent 3,096,252 dated Jul 2 1963 8752: Katsumata R, et al. Plasmids. US Patent 4,500,640 dated Feb 19 1985 10093: Pathol. Microbiol. 30: 890-899, 1967. 49855: Okumura S, et al.. Studies on the L-glutamic acid fermentation. Part I. The new bacteria of the genus-Brevibacterium isolated from the nature to produce L-glutamic acid. J. Agric. Chem. Soc. Jpn. 36: 141-159, 1962. 57836: Sung HC, et al.. Production and preparation of glutamate synthase from Brevibacterium flavum. J. Ferment. Technol. 62: 371-376, 1984.		

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Bacteria

ATCC Number:

13869

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Price:

\$150.00

Organism:

Corynebacterium glutamicum (Kinoshita et al.) Abe et al. deposited as
Brevibacterium lactofermentum Okumura et al.

Designations:

2256 [NCIB 9567]

Depositors:

Ajinomoto Co., Inc.

**Biosafety
Level:**

1

Shipped:

freeze-dried

**Growth
Conditions:**

ATCC medium: 3 Nutrient agar (Difco 0001) or nutrient broth (Difco 0003)
Temperature: 30.0 C

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Related Products

Comments:

characterization and production of L-glutamic acid [\[49855\]](#)
genes involved in lysine pathway [\[9420\]](#)

Applications:	produces glutamic acid [glutamate] [2114] [2635] [2636] [2639] [2640] [2641]
References:	2114 : Motozaki M, et al.. Process for producing L-glutamic acid by bacterial fermentation. Canadian Patent 634,377 2635 : Shio I, et al. Process for producing L-glutamic acid. US Patent 3,117,915 dated Jan 14 1964 2636 : Motozaki S, et al. Process for producing L-glutamic acid. US Patent 3,096,252 dated Jul 2 1963 2639 : Motozaki S, et al. Process for producing L-glutamic acid by bacterial fermentation. US Patent 3,128,237 dated Apr 7 1964 2640 : Okumura S, et al. Process for producing L-glutamic acid. US Patent 3,136,702 dated Jun 9 1964 2641 : Kono K, et al. Method of producing L-glutamic acid by fermentation. US Patent 3,212,994 dated Oct 19 1965 9420 : Marquez G, et al. Cloning and expression in Escherichia coli of genes involved in the lysine pathway of Brevibacterium lactofermentum. J. Bacteriol. 164: 379-383, 1985. PubMed: 2864331 32192 : Tsuchida T, et al. Process for producing L-amino acids by fermentation. US Patent 5,705,370 dated Jan 6 1998 49855 : Okumura S, et al.. Studies on the L-glutamic acid fermentation. Part I. The new bacteria of the genus Brevibacterium isolated from the nature to produce L-glutamic acid. J. Agric. Chem. Soc. Jpn. 36: 141-159, 1962.

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Bacteria

ATCC Number:

14020

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Price:

\$190.00

Organism:

Corynebacterium glutamicum (Kinoshita et al.) Abe et al. deposited as *Brevibacterium divaricatum* Su and Yamada

Designations:

[DSM 20297; NCIB 9379; NRRL B-2312]

Isolation:

soil

Depositors:

Wei-chuan Foods Corp.

History:

ATCC<<--Wei-chuan Foods Corp. <<--Y. Su and K. Yamada

Biosafety Level:

1

Shipped:

freeze-dried

Growth Conditions:

ATCC medium: 3 Nutrient agar (Difco 0001) or nutrient broth (Difco 0003)
Temperature: 30.0 C

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Type Strain:	type strain (type strain of <i>Brevibacterium divaricatum</i>)
Applications:	produces glutamic acid [glutamate] [5237] [7133]
References:	<p>5237: McCutchan WN, Hidy PH. Glutamic acid fermentation. US Patent 3,061,521 dated Oct 30 1962</p> <p>7133: Bull. Agric. Chem. Soc. Jpn. 24: 69-74, 1960.</p> <p>8943: Liebl W, et al. Transfer of <i>Brevibacterium divaricatum</i> DSM 20297T, "<i>Brevibacterium flavum</i>" DSM 20411, "<i>Brevibacterium lactofermentum</i>" DSM 20412 and DSM 1412, and <i>Corynebacterium glutamicum</i> and their distinction by rRNA gene restriction patterns. Int. J. Syst. Bacteriol. 41: 255-260, 1991. PubMed: 1713055</p> <p>32192: Tsuchida T, et al. Process for producing L-amino acids by fermentation. US Patent 5,705,370 dated Jan 6 1998</p> <p>36887: Skerman VB, et al. Approved lists of bacterial names. Int. J. Syst. Bacteriol. 30: 225-420, 1980.</p>

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